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Jc971 U.S. PTO

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PATENT  
Attorney's Docket Number: 07681.0018-01  
CUSTOMER NUMBER: 22,852

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

ASSISTANT COMMISSIONER FOR PATENTS  
Washington, D.C. 20231

Prior Application: Art Unit: 1632 Examiner: D. Crouch

SIR: This is a request for filing a

☒ Continuation ☐ Continuation-in-Part ☐ Divisional Application under 37 C.F.R. § 1.53(b) of pending prior application Serial No. 09/650,285 filed August 29, 2000 of Keith Campbell et al. for UNACTIVATED OOCYTES AS CYTOPLAST RECIPIENTS FOR NUCLEAR TRANSFER.

1. ☒ Enclosed is a complete copy of the prior application including the oath or Declaration and drawings, if any, as originally filed. I hereby verify that the attached papers are a true copy of prior application Serial No. 08/803,165 as originally filed on February 19, 1997.
2. ☐ Enclosed is a substitute specification under 37 C.F.R. § 1.125.
3. ☐ Cancel Claims \_\_\_\_.
4. ☒ A Preliminary Amendment is enclosed.
5. ☒ The filing fee is calculated on the basis of the claims existing in the prior application as amended at 3 and 4 above.

Basic Application Filing Fee					\$740	\$ 740.00
	Number of Claims		Basic	Extra Claims		
Total Claims	1	-	20		x \$18	
Independent Claims	1	-	3		x \$84	
<input type="checkbox"/> Presentation of Multiple Dep. Claim(s)					+\$270	
Subtotal						\$ 740
Reduction by 1/2 if small entity						-
TOTAL APPLICATION FILING FEE						\$ 740

LAW OFFICES

FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

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09/989128  
11/21/01

6. ☒ A check in the amount of \$740.00 to cover the filing fee is enclosed.
7. ☒ The Commissioner is hereby authorized to charge any fees which may be required including fees due under 37 C.F.R. § 1.16 and any other fees due under 37 C.F.R. § 1.17, or credit any overpayment during the pendency of this application to Deposit Account No. 06-0916.
8. ☒ Amend the specification by inserting before the first line, the sentence:

--This is a ☒ continuation of application Serial No. 09/650,285 filed August 29, 2000, which is a continuation of application Serial No. 08/803,165, filed February 19, 1997, which claims the benefit of PCT/GB96/02098, filed on August 30, 1996, and British application GB 9517779.6, filed on August 31, 1995, all of which are incorporated herein by reference.--

9. ☒ New formal drawings are enclosed.
10. ☒ The prior application is assigned of record to: Roslin Institute (Edinburgh) ; The Minister of Agriculture, Fisheries and Food; and Biotechnology & Biological Sciences Research Council.
11. ☒ Priority of application Serial Nos. PCT/GB96/02098, filed on August 30, 1996, and GB 9517779.6, filed on August 31, 1995 in Great Britain, is claimed under 35 U.S.C. § 119 or § 365. A certified copy
  - ☐ is enclosed or ☒ is on file in the prior application.
12. ☐ A verified statement claiming small entity status
  - ☐ is enclosed or ☐ is on file in the prior application.
13. ☒ An associate power of attorney in the prior application is to at least one of the following: FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P., Douglas B. Henderson, Reg. No. 20,291; Ford F. Farabow, Jr., Reg. No. 20,630; Arthur S. Garrett, Reg. No. 20,338; Donald R. Dunner, Reg. No. 19,073; Brian G. Brunsvold, Reg. No. 22,593; Tipton D. Jennings, IV, Reg. No. 20,645; Jerry D. Voight, Reg. No. 23,020; Laurence R. Hefter, Reg. No. 20,827; Kenneth E. Payne, Reg. No. 23,098; Herbert H. Mintz, Reg. No. 26,691; C. Larry O'Rourke, Reg. No. 26,014; Albert J. Santorelli, Reg. No. 22,610; Michael C. Elmer, Reg. No. 25,857; Richard H. Smith, Reg. No. 20,609; Stephen L. Peterson, Reg. No. 26,325; John M. Romary, Reg. No. 26,331; Bruce C. Zotter, Reg. No. 27,680; Dennis P. O'Reilley, Reg.

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FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

No. 27,932; Allen M. Sokal, Reg. No. 26,695; Robert D. Bajefsky, Reg. No. 25,387; Richard L. Stroup, Reg. No. 28,478; David W. Hill, Reg. No. 28,220; Thomas L. Irving, Reg. No. 28,619; Charles E. Lipsey, Reg. No. 28,165; Thomas W. Winland, Reg. No. 27,605; Basil J. Lewis, Reg. No. 28,818; Martin I. Fuchs, Reg. No. 28,508; E. Robert Yoches, Reg. No. 30,120; Barry W. Graham, Reg. No. 29,924; Susan Haberman Griffen, Reg. No. 30,907; Richard B. Racine, Reg. No. 30,415; Thomas H. Jenkins, Reg. No. 30,857; Robert E. Converse, Jr., Reg. No. 27,432; Clair X. Mullen, Jr., Reg. No. 20,348; Christopher P. Foley, Reg. No. 31,354; John C. Paul, Reg. No. 30,413; David M. Kelly, Reg. No. 30,953; Kenneth J. Meyers, Reg. No. 25,146; Carol P. Einaudi, Reg. No. 32,220; Walter Y. Boyd, Jr., Reg. No. 31,738; Steven M. Anzalone, Reg. No. 32,095; Jean B. Fordis, Reg. No. 32,984; Roger D. Taylor, Reg. 28,992; Barbara C. McCurdy, Reg. No. 32,120; James K. Hammond, Reg. No. 31,964; Richard V. Burgujian, Reg. No. 31,744; J. Michael Jakes, Reg. No. 32,824; Thomas W. Banks, Reg. No. 32,719; Christopher P. Isaac, Reg. No. 32,616; Bryan C. Diner, Reg. No. 32,409; M. Paul Barker, Reg. No. 32,013; Andrew Chanho Sonu, Reg. No. 33,457; David S. Forman, Reg. No. 33,694; Vincent P. Kovalick, Reg. No. 32,867; James W. Edmondson, Reg. No. 33,871; Michael R. McGurk, Reg. No. 32,045; Joann M. Neth, Reg. No. 36,363; Gerson S. Panitch, Reg. No. 33,751; Cheri M. Taylor, Reg. No. 33,216; Charles E. Van Horn, Reg. No. 40,266; Linda A. Wadler, Reg. No. 33,218; Jeffrey A. Berkowitz, Reg. No. 36,743; Michael R. Kelly, Reg. No. 33, 921; James B. Monroe, Reg. No. 33,971; Doris Johnson Hines, Reg. No. 34,629; Allen R. Jensen, Reg. No. 28,224; Lori Ann Johnson, Reg. No. 34,498; and David A. Manspeizer, Reg. No. 37,540.

14. ☐ The power appears in the original declaration of the prior application.
15. ☒ Since the power does not appear in the original declaration, a copy of the power in the prior application is enclosed.
16. ☒ Please address all correspondence to FINNEGAN, HENDERSON, FARABOW, GARRETT and DUNNER, L.L.P., 1300 I Street, N.W., Washington, D.C. 20005-3315. **Customer Number 22,852.**
17. ☐ Recognize as associate attorney \_\_\_\_\_
18. ☒ Also enclosed is a Request Under 37 C.F.R. §1.607 for Interference with U.S. Patent 6,235,969 to Stice et al. with Exhibits A-E.

## LAW OFFICES

FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

PETITION FOR EXTENSION. If any extension of time is necessary for the filing of this application, including any extension in the parent application, Serial No. 09/650,285, filed August 29, 2000, for the purpose of maintaining copendency between the parent application and this application, and such extension has not otherwise been requested, such an extension is hereby requested, and the Commissioner is authorized to charge necessary fees for such an extension to our Deposit Account No. 06-0916. A duplicate copy of this paper is enclosed for use in charging the deposit account.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Date: November 21, 2001

By: 

Kenneth J. Meyers

Reg. No. 25,146

Tel: (202) 408-4033

Fax: (202) 408-4400

Email: meyersk@finnegan.com

LAW OFFICES

FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: )  
)  
CAMPBELL et al. ) Group Art Unit: 1632  
)  
Serial No.: TO BE ASSIGNED ) Examiner: D. Crouch  
)  
Filed: November 21, 2001 )  
)  
For: UNACTIVATED OOCYTES AS )  
CYTOPLAST RECIPIENTS )  
FOR NUCLEAR TRANSFER )

Assistant Commissioner for Patents  
Washington, D.C. 20231

Sir:

**REQUEST UNDER 37 C.F.R. § 1.607 FOR INTERFERENCE WITH  
U.S. PATENT 6,235,969 TO STICE ET AL.**

Pursuant to the provisions of 37 C.F.R. §1.607, applicants respectfully request that an interference be declared between claim 19 in the subject application and claims 1-26 of U.S. Patent 6,235,969 to Stice et al. The patent is hereinafter referred to as "the Stice patent". A copy is attached as Exhibit A.

Applicants submit the following information in fulfillment of the requirements of 37 C.F.R. § 1.607.

I. PROPOSED COUNT

In fulfillment of the requirement of Rule 1.607(a)(2), applicants propose the following Count for purposes of interference:

A method of producing a non-human mammalian embryo by nuclear transfer comprising:

- (i) transfer of a nucleus of a non-human mammalian cell, which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle, into an unactivated, enucleated, metaphase II-arrested oocyte of the same species as the donor cell nucleus;
- (ii) activation of the recipient oocyte containing the donor cell nucleus; and
- (iii) incubation of the activated oocyte to provide an embryo;

wherein the donor cell nucleus is from a mammalian differentiated cell;

or:

- (i) transplantation of a non-human mammalian cell or a nucleus of a non-human mammalian cell into an enucleated oocyte of the same species as the donor cell or donor cell nucleus;
- (ii) activation of the recipient oocyte containing the donor cell or donor cell nucleus; and
- (iii) incubation of the activated oocyte to produce an embryo;

wherein the donor cell is a non-quiescent mammalian differentiated cell or wherein the donor nucleus is from a non-quiescent mammalian differentiated cell.

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FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

The Proposed Count incorporates the exact language of applicants' claim 19. The Proposed Count also incorporates the exact language of claim 24 of the Stice patent.<sup>1</sup>

**II. IDENTIFICATION OF PATENT CLAIMS  
CORRESPONDING TO THE PROPOSED COUNT**

Claims 1-26 of the Stice patent, which are all of the claims of the patent, are directed to methods of producing non-human mammalian embryos and to methods of cloning pigs by nuclear transfer. All of the patent claims are directed to the same invention and should be designated as corresponding to the Proposed Count. See 37 C.F.R. § 1.606.

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<sup>1/</sup> An Alternative Proposed Count could read as follows:

A method of cloning a non-human mammal by nuclear transfer comprising the method of claim 19 of Campbell et al.'s application Serial No. \_\_\_\_\_ or claim 24 of Stice et al.'s U.S. Patent No. 6,235,969.

**III. IDENTIFICATION OF APPLICANTS' CLAIMS  
CORRESPONDING TO THE PROPOSED COUNT**

Applicants' claim 19 is also directed to methods of producing non-human mammalian embryos by nuclear transfer. This claim should be designated as corresponding to the Proposed Count.

**IV. APPLICATION OF APPLICANTS' CLAIM  
TO THE DISCLOSURE IN THEIR APPLICATION**

Applicants' claim 19 is being presented in a Preliminary Amendment filed herewith. Section (a)(5) of Rule 1.607 requires applicants to identify support in their application for any of their claims designated as corresponding to the Proposed Count.

Exhibit B annexed hereto contains each of the recitations in applicants' claim 19 and quotations from the specification supporting each recitation. Exhibit B thus satisfies the requirement of Rule 1.607(a)(5).

**V. APPLICANTS ARE THE SENIOR PARTY RELATIVE TO STICE ET AL.**

The Stice patent is based on a U.S. application filed July 3, 1997. The Stice patent is related to an earlier application filed on January 10, 1997. If Stice et al. can



demonstrate that they are entitled to the benefit of the filing date of each of the earlier-filed applications as constructive reductions to practice, Stice et al.'s effective filing date for purposes of an interference would be January 10, 1997.

Applicants, on the other hand, have an effective U.S. filing date of August 31, 1995, through a series of priority applications, each of which constitutes a constructive reduction to practice of the Proposed Count. Specifically, the subject application is a continuation of parent application Serial No. 09/650,194, filed August 29, 2000, which is a continuation of grandparent application Serial No. 08/803,165, filed February 19, 1997. Thus, applicants are entitled to the benefit of the filing date of February 19, 1997, of the grandparent application because it is linked to the grandparent application through a continuation application, and thus has an identical specification to the grandparent application. 35 U.S.C. § 120.

The grandparent application, in turn, is a §371 application of PCT/GB96/02098, filed August 30, 1996. A copy of the PCT application as published under No. WO 97/07668 is attached as Exhibit C. The PCT application and the subject application are identical. Thus, applicants are also entitled to the benefit of

LAW OFFICES

FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

the filing date of August 30, 1996, of the PCT application. 35 U.S.C. § 119 and MPEP 1896.

Finally, the PCT application claims the benefit of British application No. 95 17779.6, filed August 31, 1995. A certified copy of the British priority application is of record in application Serial No. 08/803,165, filed February 19, 1997.

There are several differences between the British priority application and the subject U.S. application. These differences have been highlighted on Exhibit D, which is a copy of the subject application. It will be evident that the highlighted passages do not affect applicants' right to the benefit of the British application for the subject matter of claim 19 in the subject application. Thus, applicants are entitled to the filing date of their British priority application. 35 U.S.C. § 119.

In summary, applicants' effective filing date of August 31, 1995, can be traced from the subject continuation application through the parent and grandparent applications to the earlier PCT application and finally to the British priority application. Each of these applications constitutes a constructive reduction to practice of the Proposed Count. Because applicants' effective filing date of **August 31, 1995**, predates by **almost 17**

months the earliest filing date of **January 10, 1997**, which Stice et al. could allege, justice requires that applicants be named the senior party in any interference that may be declared with the Stice patent.

**VI. APPLICANTS AND STICE ET AL. ARE CLAIMING THE SAME PATENTABLE INVENTION**

Applicants' claim 19 defines the same patentable invention as claims 1-26 in the Stice patent. Thus, interference-in-fact exists. See 37 C.F.R. § 1.601(j). ("An interference-in-fact exists when at least one claim of a party that is designated to correspond to a count and at least one claim of an opponent that is designated to correspond to the count define the same patentable invention.")

More particularly, 37 C.F.R. § 1.601(n) provides that one invention is "the same patentable invention" as another invention when the first invention is the same as (35 U.S.C. § 102) or is obvious (35 U.S.C. § 103) in view of the second invention, assuming the second invention is prior art with respect to the first invention.

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FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

Recent precedent of the Trial Section of the Interference Division of the Board of Patent Appeals and Interferences indicates that resolution of whether an interference-in-fact exists involves a two-way patentability analysis. According to the Board.

The claimed invention of Party A is presumed to be prior art vis-a-vis Party B and vice versa. The claimed invention of Party A must anticipate or render obvious the claimed invention of Party B and the claimed invention of Party B must anticipate or render obvious the claimed invention of Party A. When the two-way analysis is applied, then regardless of who ultimately prevails on the issue of priority, \* \* \* [USPTO] assures itself that it will not issue two patents to the same patentable invention.

*Winter v. Fujita*, 53 U.S.P.Q.2d 1234, 1243 (Bd. Pat. App. & Intf. 1999), reh'g denied, 53 U.S.P.Q.2d 1478 (Bd. Pat. App. & Intf. 2000).

In support of their request for declaration of an interference, applicants will describe their invention and then compare the terms in Stice et al.'s claim 24 with the corresponding terms in applicants' claim 19. This comparison will convincingly show that applicants are claiming the same patentable invention as that claimed in the Stice patent and that interference-in-fact exists.

Applicants will then show that applicants have met the one year time limit imposed by 35 U.S.C. § 135(b) by claiming this invention within one year of the issuance of the Stice patent.

A. APPLICANTS' PIONEERING WORK INVOLVING NUCLEAR TRANSFER INTO DIFFERENTIATED CELLS LEAD TO THE CLONING OF "DOLLY" THE SHEEP

The report of the cloning of "Dolly" the sheep generated enormous attention in the scientific and general press because of its novelty and the significance of the work. This cloning work is the subject of applicants' invention.

At the time of applicants' invention, animal cloning had been achieved by genetic manipulation using nuclear transfer technology: A nucleus was removed from a donor cell, then transplanted into an oocyte whose own nucleus had previously been removed. The resulting renucleated oocyte gave rise to an animal that carried the nuclear genome of only the donor of the nucleus. The individual providing the donor nucleus and the individual that developed from the renucleated oocyte were referred to as "clones".

Nuclear transfer technology first employed a donor cell that was derived from an early embryo. The cells of the embryo had not undergone substantial division and differentiation ---

the cells were totipotent, meaning that they had the potential to develop into any type of cell in an adult.

Unlike embryo cloning, the prospect of cloning a cell from an adult seemed remote. More particularly, all animals develop from a single cell, the fertilized ovum, which gives rise to the various tissues and organs. Cells from the ovum undergo division and differentiation, which is driven by gene switching: The difference between one cell type and another is primarily in the range of genes that are active in each cell. Certain genes in the genome are "programmed" to express their proteins, leading to cell specialization at a very early stage of development within the embryo.

It was thought that a differentiated cell was committed to a specialized course of development and ultimately a specialized function. It was believed that a differentiated cell exhibited a memory for its specialized function and passed its functional characteristics on to its progeny. Prior to applicants' invention, it was thought that once a cell became differentiated and entered a determined developmental pathway, the pathway was irreversible. No manipulation of the cell environment would, for example, cause a heart cell to differentiate into a liver cell.

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FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N.W.  
WASHINGTON, DC 20005  
202-408-4000

Applicants' specification describes the cause of this phenomenon as follows: "During development certain genes become imprinted i.e., are altered such that they are no longer transcribed." (Specification at page 4, lines 16-18.) Applicants discovered that the "imprint" on an adult differentiated cell can indeed be removed by "reprogramming" the cell nucleus following its transfer to the enucleated, recipient oocyte. The application of this discovery produced "Dolly" the sheep in Example 2 in the subject application by nuclear transfer from an adult differentiated cell in the G<sub>0</sub> phase of the cell cycle.

More particularly, as described in the present application, the nucleus that is transferred to the enucleated, recipient oocyte can be taken from an adult differentiated cell. "Dolly" the sheep was produced in Example 2 using a nucleus from an adult sheep cell in the G<sub>0</sub> phase of its cell cycle. The specification teaches that an adult differentiated cell in the G<sub>1</sub> phase of its cell cycle could be used as well. (See pages 16-21, *infra*, for a more detailed discussion of the cell cycle.) Nuclear transfer from the adult differentiated cell into an oocyte arrested in metaphase II gave rise to a viable sheep embryo by maintaining normal ploidy (i.e. diploidy). Activating

the embryo after nuclear transfer allowed the nucleus to remain exposed to the recipient cytoplasm. This delay resulted in nuclear reprogramming so that the renucleated oocyte could be implanted in a live animal and could develop to term.

The successful cloning of "Dolly" showed, for the first time, that the nucleus from a differentiated adult cell could be reprogrammed to become totipotent once more, just like the genetic material in the fertilized oocyte from which the donor cell had ultimately developed. This successful cloning of an adult animal forced scientists to accept that genome modifications, once considered irreversible, can be reversed, and that genomes of adult cells can be reprogrammed by factors in the oocyte to make them capable once again of differentiating into any cell type.

Applicants' claim 19 is directed to a method of producing a non-human mammalian embryo by nuclear transfer using a differentiated cell from an adult donor. The resulting embryos, after implantation into a host animal, can develop into a live animal in a manner similar to the birth of "Dolly".

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FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000



**B. STICE ET AL. ALSO CLAIM TO HAVE  
INVENTED ANIMAL CLONING BY NUCLEAR  
TRANSFER USING DIFFERENTIATED CELLS**

The Stice patent also claims a method of cloning a non-human mammal by nuclear transfer using a differentiated cell. Stice et al. describe their work as follows:

According to the invention, cell nuclei derived from differentiated pig cells are transplanted into enucleated pig oocytes. The nuclei are reprogrammed to direct the development of cloned embryos, which can then be transferred into recipient females to produce fetuses and offspring, or used to produce CICM cells. The cloned embryos can also be combined with fertilized embryos to produce chimeric embryos, fetuses and/or offspring.

(Exhibit A at col. 6, lines 41-47.)

The importance of differentiated cells for nuclear transfer is pointedly emphasized in the Stice patent: "Again the present invention is novel because differentiated cell types are used."

(Exhibit A at col. 9, lines 18-19.)

The use of "differentiated cells" was characterized as "novel" and the essence of their work. Stice et al. were apparently unaware of applicants' work using differentiated cells in nuclear transfer when Stice et al. filed their application.

**C. APPLICANTS' CLAIMED INVENTION IS THE SAME AS THE SUBJECT MATTER OF THE STICE ET AL. AS SHOWN BY A COMPARISON OF APPLICANTS' CLAIM 19 WITH CLAIM 24 OF THE STICE PATENT.**

Table 2 and the comments that follow show that applicants' claim 19 contains limitations that are the same as limitations in claim 24 of the Stice patent. These are the two claims that comprise applicants' Proposed Count on pages 2-3, *supra*.

**TABLE 2**

**COMPARISON OF APPLICANTS' CLAIM 19 WITH CLAIM 24 OF THE STICE PATENT.**

<b>Applicants' claim 19</b>	<b>Claim 24 of the Stice patent</b>
19. A method of producing	19. A method of producing
a non-human mammalian embryo	a non-human mammalian embryo
by nuclear transfer	by nuclear transfer
comprising:	comprising:
(i) transfer	(i) transplantation
of a nucleus	of a . . . nucleus
of a non-human	of a non-human
mammalian cell,	mammalian cell
which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle,	
into an	into an
unactivated,	
enucleated,	enucleated
metaphase II-arrested	
oocyte	oocyte
of the same species as the donor cell nucleus;	of the same species as the . . . donor cell nucleus <sup>2</sup> ,
(ii) activation	activation

Applicants' claim 19	Claim 24 of the Stice patent
of the recipient oocyte containing the donor cell nucleus; and	of the recipient oocyte containing the . . . donor cell nucleus; and
(iii) incubation	incubation
of the activated oocyte	of the activated oocyte
to provide an embryo;	to produce an embryo;
wherein the donor cell nucleus	wherein . . . the donor nucleus <sup>3</sup>
is from a	is from a
	non-quiescent
mammalian	mammalian
differentiated cell.	differentiated cell.

3 The complete clause in Stice claim 24 reads as follows:  
"wherein the donor cell is a non-quiescent mammalian  
differentiated cell or wherein the donor nucleus is from a non-  
quiescent mammalian differentiated cell." (Exhibit A at col.  
20, lines 59-61.)

It will be evident from Table 2 that applicants' claim 19 contains recitations that are identical to recitations in claim 24 of the Stice patent. As described in Exhibit B attached hereto, all of these recitations are supported by applicants' specification. Support for these recitations in applicants claim will not be further discussed.

Instead, the terms in applicants' claim that are absent from Stice et al.'s claim, or appear to be different, will now be discussed. These terms are arranged below in a different order than they appear in Table 2 to facilitate an understanding of the meaning of the terms and their relation to each other. This discussion will leave no doubt that applicants and Stice et al. are claiming the same invention and that interference-in-fact exists.

(1) The recitation of a nuclear donor cell  
"which has passed start in the mitotic cell  
cycle and is in the G1 phase of the cell  
cycle" in applicants' claim

vs.

the recitation of a "non-quiescent" cell in  
Stice et al.'s claim

The nucleus for cloning the non-human mammal is taken from a particular type of non-human mammalian cell, which is referred to herein as the "nuclear donor" for the sake of brevity. Specifically, in applicants' claim 19, the nuclear donor is a cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle." Stice et al.'s nuclear donor is a cell that is "non-quiescent." The use of these terms does not impart separate patentability to either claim. Each term describes a cell that is actively dividing.

The prosecution history of related Stice U.S. Patent 6,215,041 makes it clear that Stice et al. understood that a "non-quiescent" cell is an "actively dividing" cell. Dr. James M. Robl, one of the Stice et al. inventors, stated that:

(7) In particular, the novel developments discovered by the inventors of this application include:

(i) the successful use of cells committed to a somatic cell lineage for nuclear transfer or transplantation;

(ii) the successful use of actively dividing, i.e., non-quiescent cells for nuclear transplantation; and

(iii) the use of somatic cell genetic modification to produce genetically modified animals.

(Exhibit E, Declaration of James M. Robl, Ph.D. Pursuant To 37 C.F.R. §1.132 at page 3; original emphasis.)

Just as the "non-quiescent" nuclear donor cell recited in Stice et al.'s claim is "actively dividing", applicants' nuclear donor cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle" is "actively dividing." Underlying the meaning of a nuclear donor cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle in applicants' claim is an understanding of the cell cycle and an appreciation for the limited number of phases in

the cycle. The mitotic cell cycle is described in applicants' specification as follows.

The mitotic cell cycle has four distinct phases, G1, S, G2, and M. The beginning event in the cell cycle, called start, takes place in the G1 phase and has a unique function. The decision or commitment to undergo another cell cycle is made at start. Once a cell has passed through start, it passes through the remainder of the G1 phase, which is the pre-DNA synthesis phase.

The second stage, the S phase, is when DNA synthesis takes place. This is followed by the G2 phase, which is the period between DNA synthesis and mitosis. Mitosis itself occurs at the M phase. Quiescent cells (which include cells in which quiescence has been induced as well as those cells which are naturally quiescent, such as certain fully differentiated cells) are generally regarded as not being in any of these four phases of the cycle; they are usually described as being in a G0 state, so as to indicate that they would not normally progress through the cycle. (Applicants' specification at page 7, line 26 to page 8, line 11.) It is evident from this description that there are only four phases in the mitotic cell cycle, namely, the G1, S, G2, and M phases.

Once a cell enters the mitotic cell cycle by passing through "start", the cell is committed to pass through the remainder of the G1 phase of the cell cycle in which the cell is actively dividing. These are the conditions recited in applicants' claim 19. This claim recites that the nuclear donor is a cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle."

Instead of reciting that the nuclear donor is a cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle," Stice et al.'s claim 24 recites that the donor cell is "non-quiescent". By not indicating which stage of the cell cycle the "non-quiescent" cell is in, claim 24 of the Stice patent reads on a nuclear donor cell in any phase of the cell cycle, namely, the G1, S, G2, or M phase. Thus, the difference between the two terms is that applicants' claim reads on the use of a nuclear donor cell actively dividing in the G1 phase of the cell cycle, whereas Stice et al.'s claim reads on a nuclear donor cell actively dividing in any one of the four phases of the cell cycle, including the G1 phase.

Applying the analysis required by the *Winter v. Fujita* case, applicants' species of an actively dividing nuclear donor cell "which has passed start in the mitotic cell cycle and is in

the G1 phase of the cell cycle" anticipates the Stice et al. claim embracing a "non-quiescent" nuclear donor cell that is actively dividing in any one of the four phases of the cell cycle, assuming applicants' claim is prior art to Stice et al.'s claim and all of the other claim limitations are the same. A later genus claim is never patentable over an earlier species claim. *Eli Lilly v. Barr Laboratories, Inc.*, 222 F.3d 973, 976 (Fed. Cir. 2000).

Following a similar analysis, but assuming the Stice et al. claim is prior art to applicants' claim, applicants' claim to the use of an actively dividing nuclear donor cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle" would be rendered *prima facie* obvious by Stice et al.'s claim encompassing the use of an actively dividing nuclear donor cell in one of the four phases of the cell cycle. Indeed, applicants' claim to one phase of the cell cycle may be anticipated by Stice et al.'s claim embracing a nuclear donor cell in any one of the four phases, one of which is recited in applicants' claim, because it is well established that a small genus can anticipate a species within that genus. See, e.g., *In re Petering*, 301 F.2d 676, 682, 133 U.S.P.Q. 275, 280 (C.C.P.A. 1962) (Genus of 20 compounds describes each species within the



meaning of § 102(b)); *In re Schaumann*, 572 F.2d 312, 316-317, 197 U.S.P.Q. 5, 9 (C.C.P.A. 1978) (Prior art disclosure embraces such a limited number of compounds closely related to one another in structure that it "provides a description of those compounds just as surely as if they were identified in the reference by name.").

In any event, the recitation of a donor cell "which has passed start in the mitotic cell cycle and is in the G1 phase of the cell cycle" in applicants' claim and the recitation of a donor cell that is "non-quiescent" in Stice et al.'s claim do not impart patentable distinctness to either claim. Both types of donor cells are "actively dividing." Thus, one claim anticipates the other claim, while the other claim at the least renders the first claim *prima facie* obvious.

(2) **The recitation of "metaphase II - arrested" in applicants' claim**

Applicants' claim contains another recitation that is absent from Stice et al.'s claims, namely, that the oocyte into which the nucleus from the nuclear donor is transferred is in a particular phase of its cell cycle. It is "metaphase II-arrested." The absence of this term from Stice et al.'s claim is immaterial for determining "same patentable invention".

Stice et al. teach in their specification that metaphase-II oocytes should be used for successful nuclear transfer.

Specifically, Stice et al. state that:

Additionally, metaphase II stage oocytes, which have been matured in vivo have been successfully used in nuclear transfer techniques.

\* \* \*

The stage of maturation of the oocyte at nucleation and nuclear transfer has been reported to be significant to the success of NT methods. (See e.g., Prather et al., *Differentiation*, 48, 1-8, 1991). In general, successful mammalian embryo cloning practices use the metaphase II stage oocyte as the recipient oocyte because at this stage it is believed that the oocyte can be or is sufficiently "activated" to treat the introduced nucleus as it does a fertilizing sperm.

(Exhibit A at col. 9, lines 41-56.)

According to Stice et al., oocytes in metaphase II are the cells of choice to ensure successful nuclear transfer.

Moreover, Stice et al. indicate this was known in the art.

The identification of a "metaphase II-arrested" oocyte as the recipient of the nucleus from the non-quiescent differentiated cell in the G1 phase of the cell cycle in applicants' claim and the absence of this recitation from Stice et al.'s claim does not impart separate patentability to either claim applying the analysis under *Winter v. Fujita*.

Specifically, assuming applicants' claim is prior art to Stice

et al.'s claim and all of the other claim limitations are the same, applicants' claim would anticipate the claim of Stice et al.; applicants' claim would contain all of the limitations of the claim of Stice et al., and the additional limitation "metaphase II-arrested" oocyte in applicants' claim would not change the analysis.

Applying the test in reverse, and assuming the Stice et al. claim is prior art to applicants' claim and that all of the other limitations are the same, the recitation of a "metaphase II-arrested" oocyte in applicants' claim would have been obvious in view of the Stice et al. claim taken in view of the knowledge in the art that a metaphase II oocyte was the cell of choice for nuclear transfer.

**(3) The recitation of "unactivated" in applicants' claim**

Following transfer of the nucleus into the enucleated oocyte and reprogramming of the genes of the donor nucleus, the resulting renucleated oocyte is activated to resume embryonic development. Applicants and Stice et al. each require a step of "activating" the resulting reconstructed embryo or NT unit in their claims.

Applicants' claim also recites that the enucleated oocyte is "unactivated" at the time of the nucleus is transferred from the nuclear donor. While the term "unactivated" is not recited in Stice et al.'s claim, it is inherent in the claim as the claim requires "activation of the recipient oocyte." If the oocyte had already been activated, this activation step would be unnecessary.

In addition, if the oocyte had already been activated, the claim of Stice et al. should have included a step of interrupting activation in order to give meaning to the subsequent step of "activation of" the resultant renucleated oocyte. The Stice et al. claim does not include a step of interrupting activation of an activated oocyte, and accordingly, the only reasonable interpretation of the claim is that the oocyte is "unactivated" when the nucleus is transferred.

The term "unactivated" oocyte, which is inherent in Stice et al.'s claim, does not patentably distinguish the claim from applicants' claim, or vice versa.

In summary, the comparison of applicants' claim 19 with claim 24 of the Stice et al. patent shows that most of the claim limitations are identical and those that are not do not impart separate patentability to either claim. The only conclusion is

that these two claims define the same patentable invention and that interference-in-fact exists.

**D. APPLICANTS HAVE MET THE ONE YEAR TIME LIMIT  
IMPOSED BY 35 U.S.C. § 135(b) BY CLAIMING THE SAME  
PATENTABLE INVENTION AS STICE ET AL. WITHIN ONE  
YEAR AFTER THE STICE PATENT ISSUED**

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The Stice et al. patent issued on **May 22, 2001**. Applicants are presenting claim 19 in the subject application in the Preliminary Amendment filed herewith. Applicants thus claimed the interfering subject matter within one year after the Stice patent issued, thereby meeting the one-year time limit imposed by 35 U.S.C. § 135(b).

**VII. CONCLUSION**

It is a fundamental principle that issuance of two patents for inventions that are either identical to or not patentably distinct from each other must be avoided. M.P.E.P. 2306, *citing Aelony v. Arni*, 547 F.2d 566, 192 U.S.P.Q. 486 (C.C.P.A. 1997). This mandate has a matter of urgency attached to it in the present case in which a patent has already been issued to an entity that would be the junior party in an interference with applicants. An interference should be declared, and applicants should be designated as the senior party in the interference.

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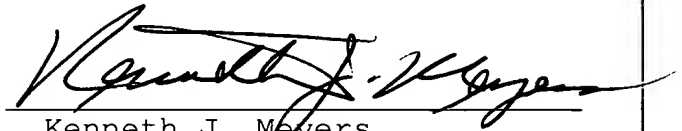
FINNEGAN, HENDERSON,  
FARABOW, GARRETT,  
& DUNNER, L.L.P.  
1300 I STREET, N. W.  
WASHINGTON, DC 20005  
202-408-4000

If there are any fees due in connection with the filing of this Request, please charge such fees to our Deposit Account No. 06-0916.

Respectfully submitted,  
FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

Date: November 21, 2001

By:



Kenneth J. Meyers  
Reg. No. 25,146  
Tel: (202) 408-4000  
Fax: (202) 408-4400  
Email:  
ken.meyers@finnegan.com

235451